

BMJ Open Influence of family history on the willingness of outpatients to undergo genetic testing for salt-sensitive hypertension: a cross-sectional study

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ABSTRACT

Objectives It is unclear whether family medical history influences the willingness to undergo genetic testing. This study aimed to determine how family history affected the willingness to undergo genetic testing for salt-sensitive hypertension in patients with and without hypertension.

Design Cross-sectional study using a self-administered questionnaire.

Setting Six primary care clinics and hospitals in Japan.

Participants Consecutive 1705 outpatients aged >20 years, 578 of whom had hypertension.

Primary and secondary outcome measures The primary outcome variable was the willingness to undergo genetic testing to determine the risk of salt-sensitive hypertension, and the secondary variables were age, sex, education level, family history and concerns about hypertension. Factors associated with a willingness to undergo genetic testing were evaluated in patients with and without hypertension using a logistic regression model.

Results In the hypertension and non-hypertension groups, 323 (55.9%) and 509 patients (45.2%), respectively, were willing to undergo genetic testing. This willingness was related with a high level of education (adjusted OR (ad-OR): 1.81, 95% CI 1.12 to 2.93), family history of stroke (1.55, 1.04 to 2.31) and concerns about hypertension (2.04, 1.27 to 3.28) in the hypertension group, whereas in the non-hypertension group, it was influenced by education level (ad-OR: 1.45, 95% CI 1.13 to 1.86), family history of hypertension (1.52, 1.17 to 1.98) and concerns about hypertension (2.03, 1.53 to 2.68).

Conclusions The influence of family history on the willingness to undergo genetic testing for risk of salt-sensitivity hypertension differed between participants with and without hypertension. In particular, participants without hypertension wished to know their likelihood of developing hypertension, whereas those with hypertension were interested to know the risk of stroke (a complication of hypertension). Family history could help better counsel patients about genetic testing on the basis of their medical history.

INTRODUCTION

Family history is the most important tool in diagnosing and assessing risk in medical

Strengths and limitations of this study

- Logistic regression analyses were performed to examine the associations between family history and willingness to undergo genetic testing in patients with and without hypertension.
- The generalisability of the results may not extend to non-Japanese populations.
- This study used self-reported data, which might have introduced information bias.
- Unidentified confounding factors may have affected the association between the willingness to undergo genetic testing and family medical history.

genetics, and it serves as a critical element in the use of predictive genetic testing in primary care.¹ In particular, a family history of hypertension is significantly associated with primary hypertension.^{2–4} Although knowledge of patient genetics is useful in making decisions regarding treatment, patients are often ill prepared for such tests.⁵ Nevertheless, when patients with chronic disease seek information on their genetics or genetic testing, their general practitioner should provide such information.⁵

The recent completion of the human genome project and the current research on single nucleotide polymorphisms led to the identification of genetic mutations that increase the risk of common diseases such as cardiovascular disease, diabetes and cancer.⁶ Moreover, direct-to-consumer genetic testing services provided by private companies are rapidly gaining popularity.⁷ However, consumers have concerns regarding possible adverse consequences of genetic testing, particularly privacy issues and discrimination in health insurance and employment.⁸ Furthermore, because the clinical outcome of genomic medicine interventions for common chronic diseases is still unclear,

physicians also have misgivings regarding genetic testing and seem reluctant to recommend it.⁸ Typically, prospective users are worried about the onset of diseases such as breast cancer and ovarian cancer.^{9–10} Genetic testing has merits and demerits in this regard; despite the predictive capability, it is limited in terms of clinical validity and has unknown clinical utility.^{11–12} The prerequisites of the use of genetic testing for primary care include understanding the current limitations of this approach and possible consequences of its commercial over-the-counter application; the primary care team may identify those who they believe will benefit from further discussion about their family history.¹³

Several gene polymorphisms associated with salt-sensitive hypertension have been identified.^{14–16} Patients with these genetic factors are likely to develop hypertension from excessive salt intake.¹⁴ Moreover, hypertension is a risk factor for stroke and myocardial infarction.^{17–19} We previously reported that family history of hypertension was an independent factor positively related to the willingness of outpatients to undergo genetic testing for salt-sensitive hypertension.²⁰ However, the effects of family history might differ in patients with and without hypertension. In this study, we evaluated the association between family history and willingness to undergo genetic testing for salt-sensitive hypertension in patients with and without hypertension; we expect that the results of this study could help respond to the misgivings of physicians and help them to deal appropriately with family history information during genetic counselling.

METHODS

Study design

This was a cross-sectional study that used a self-administered questionnaire.

Participants and settings

We enrolled consecutive outpatients aged >20 years who visited the primary care departments of four clinics and two small hospitals in Japan.

Measurements

We collected data during 2-week periods at each clinic or hospital between September 2009 and February 2010. The patients received the questionnaire from research assistants at reception and answered it in the waiting room after being informed that they could decline participation without incurring any penalty and that they would not be remunerated for participation. Whether patients answered the questionnaire was not revealed to the primary care physicians. The questionnaire included questions on the patient's age, sex, education level, family and personal medical history (with regard to hypertension, diabetes mellitus, stroke and myocardial infarction), body mass index (BMI), concerns pertaining to hypertension and diabetes mellitus ('Do you worry about developing hypertension?' and 'Do you worry about developing diabetes mellitus?', respectively), salt preferences

('Do you prefer salty foods?'), current lifestyle (smoking, drinking, regular exercise and reduced salt intake) and willingness to undergo genetic testing for salt-sensitive hypertension ('Would you prefer to undergo a genetic test to determine whether you are genetically predisposed to hypertension due to excessive salt intake?'). We provided a description of the genetic test for salt-sensitive hypertension ('This test examines the presence of the salt-sensitive gene that tends to cause salt retention in the body, leading to hypertension.') but no additional information.

Statistical analysis

We divided the participants into two groups, with and without hypertension, based on the presence of hypertension in the self-reported medical history. Before descriptive analysis, participants were divided into three categories by age (<50, 50–64 and ≥65 years). Obesity was defined as a BMI >25 kg/m², according to the criteria of obesity in Japan and Asia-Oceania.²¹ Continuous data for age are expressed as mean±SD, and categorical data for all other variables are expressed as proportions. For testing, t-tests and χ^2 tests were used to compare age and proportions of participants between the groups with and without hypertension, respectively.

Logistic regression analyses were conducted to determine factors related to the willingness to undergo genetic testing for each patient. For these analyses, the patients were divided dichotomously in two groups on the basis of age (≥50 years and <50 years). Patients who had graduated from a college or university were classified into the higher education group, while all others were classified into the non-higher education group. In univariate analysis, crude ORs and 95% CIs were calculated for age, sex, education level, occupation, family medical history, personal medical history, obesity, concerns about hypertension and diabetes mellitus and salt preferences. Adjusted ORs (ad-ORs; 95% CI) were then calculated by adjusting for variables that were significantly associated in the univariate analyses. The significance threshold was set at 0.05. Statistical analysis was performed using STATA/SE, V.11.2.

Ethics

The Bioethics Committee of Jichi Medical University approved this study.

RESULTS

Of the 2237 outpatients, 1705 (76.2% response rate) completed the questionnaire and were included in the study. Mean age of all participants was 57.5±17.6 years (males: 607; 35.6%). The numbers of participants with and without hypertension were 578 (33.9%) and 1127 (66.1%), respectively; 323 (55.9%) participants with hypertension and 509 (45.2%) participants without hypertension were willing to undergo genetic testing. The mean age differed between the two groups (with hypertension: 69.6±12.4 years; without hypertension:

Table 1 Characteristics of participants who completed the questionnaire (n=1705)

	No hypertension (n=1127)	Hypertension (n=578)	p Value
Age (years), mean±SD	51.3±16.6	69.6±12.4	<0.001
<50	548 (48.6)	40 (6.9)	<0.001
50–64	301 (26.7)	145 (25.1)	
≥65	278 (24.7)	393 (68.0)	
Sex			0.083
Male	385 (34.2)	222 (38.4)	
Female	742 (65.8)	356 (61.6)	
Education			
Elementary school	39 (3.5)	71 (12.3)	<0.001
Junior high school	210 (18.6)	198 (34.3)	
High school	435 (38.6)	208 (36.0)	
College	310 (27.5)	65 (11.2)	
University	133 (11.8)	36 (6.2)	
Family history			
Hypertension	361 (32.0)	291 (50.3)	<0.001
Diabetes mellitus	173 (15.4)	70 (12.1)	0.070
Stroke	151 (13.4)	146 (25.3)	<0.001
Myocardial infarction	91 (8.1)	57 (9.9)	0.22
Medical history			
Diabetes	78 (6.9)	110 (19.0)	<0.001
Stroke	11 (1.0)	22 (3.8)	<0.001
Myocardial infarction	17 (1.5)	22 (3.8)	0.003
Physical examination findings			
Obesity (BMI >25 kg/m ²)	177 (15.7)	159 (27.5)	<0.001
Concerns about			
Hypertension	432 (38.3)	489 (84.6)	<0.001
Diabetes	500 (44.4)	297 (51.4)	0.004
Individual preferences			
Salt preference	638 (56.6)	351 (60.7)	0.10
Current lifestyle			
Smoking	204 (18.1)	64 (11.1)	<0.001
Drinking	477 (42.3)	209 (36.2)	0.014
Regular exercise	376 (33.4)	288 (49.8)	<0.001
Reduced salt intake	504 (44.7)	421 (72.8)	<0.001
Attitude towards genetic testing			
Willingness to undergo	509 (45.2)	323 (55.9)	<0.001

Data are presented as N (%) or mean±SD.
BMI, body mass index.

51.3±16.6 years). Similarly, the proportions with and without hypertension differed according to age; education level; family history of hypertension and stroke; medical history of diabetes, stroke and myocardial infarction; presence of obesity; concerns about hypertension and diabetes; current smoking and drinking;

regular exercise; reduced salt intake; and desire to undergo a genetic test differed significantly between the groups (table 1).

In the univariate analysis, the factors associated with a willingness to undergo genetic testing for participants without hypertension were higher education (crude OR,

Table 2 Univariate analysis of associations between measured variables and willingness to undergo a genetic test in patients without hypertension

	Willing (n=509) (%)	Not willing (n=618) (%)	OR	95% CI	p
Age, years					
≥50	275 (54.0)	304 (49.2)	1.21	(0.96 to 1.54)	0.11
Sex					
Male	166 (32.6)	219 (35.4)	0.88	(0.69 to 1.13)	0.32
Education					
Higher (at least college)	224 (44.0)	219 (35.4)	1.43	(1.13 to 1.82)	0.003
Family history					
Hypertension	196 (38.5)	165 (26.7)	1.72	(1.34 to 2.21)	<0.001
Diabetes mellitus	81 (15.9)	92 (14.9)	1.08	(0.78 to 1.50)	0.63
Stroke	76 (14.9)	75 (12.1)	1.27	(0.90 to 1.79)	0.17
Myocardial infarction	39 (7.7)	52 (8.4)	0.90	(0.59 to 1.39)	0.64
Medical history					
Diabetes	41 (8.1)	37 (6.0)	1.38	(0.87 to 2.17)	0.17
Stroke	8 (1.6)	3 (0.5)	3.27	(0.78 to 19.24)	0.065*
Myocardial infarction	7 (1.4)	10 (1.6)	0.85	(0.33 to 2.17)	0.74
Physical findings					
Obesity (BMI >25kg/m ²)	82 (16.1)	95 (15.4)	1.06	(0.77 to 1.46)	0.73
Concerns about					
Hypertension	247 (48.5)	185 (29.9)	2.21	(1.73 to 2.82)	<0.001
Diabetes	253 (49.7)	247 (40.0)	1.47	(1.16 to 1.87)	0.001
Individual preferences					
Salt preference	300 (58.9)	338 (54.7)	1.19	(0.94 to 1.51)	0.15
Current lifestyle					
Smoking	83 (16.3)	121 (19.6)	0.80	(0.59 to 1.09)	0.16
Drinking	222 (43.6)	255 (41.3)	1.10	(0.87 to 1.40)	0.43
Regular exercise	169 (33.2)	207 (33.5)	0.99	(0.77 to 1.27)	0.92
Reduced salt intake	230 (45.2)	274 (44.3)	1.03	(0.82 to 1.31)	0.78

*Fisher's exact test.

BMI, body mass index.

1.43; 95% CI 1.13 to 1.82), a family history of hypertension (crude OR: 1.72; 95% CI 1.34 to 2.21) and concerns about hypertension (crude OR, 2.21; 95% CI 1.73 to 2.82) or diabetes mellitus (crude OR, 1.47; 95% CI 1.16 to 1.87) (table 2).

In participants with hypertension, such factors were higher education (crude OR, 2.11; 95% CI 1.33 to 3.35), a family history of hypertension (crude OR, 1.50; 95% CI 1.08 to 2.09) or stroke (crude OR, 1.60; 95% CI 1.09 to 2.36) and concerns about hypertension (crude OR, 2.34; 95% CI 1.47 to 3.71) (table 3).

Multivariate logistic regression analysis (table 4) revealed that higher education (ad-OR, 1.45; 95% CI 1.13 to 1.86), a family history of hypertension (ad-OR, 1.52; 95% CI 1.17 to 1.98) and concerns about hypertension (ad-OR, 2.03; 95% CI 1.53 to 2.68) were the factors independently associated with the willingness to undergo

genetic testing in participants without hypertension, whereas in those with hypertension such factors were higher education (ad-OR, 1.81; 95% CI 1.12 to 2.93), a family history of stroke (ad-OR: 1.55; 95% CI 1.04 to 2.31) and concerns about hypertension (ad-OR, 2.04; 95% CI 1.27 to 3.28).

DISCUSSION

This study shows that a willingness to undergo genetic testing is affected by family history of stroke and hypertension in individuals with and without hypertension, respectively, demonstrating a difference in the motivation to undergo genetic testing for salt-sensitive hypertension between these two groups. Furthermore, we found that the extent of distress regarding developing an illness depends on the present stage of the disease. Physicians

Table 3 Univariate analyses of associations between measured variables and willingness to undergo a genetic test in patients with hypertension

	Willingness (n=323) (%)	No willingness (n=255) (%)	OR	95% CI	p
Age, years					
≥50	299 (92.6)	239 (93.7)	0.83	(0.44 to 1.59)	0.59
Sex					
Male	125 (38.7)	97 (38.0)	1.03	(0.73 to 1.44)	0.87
Education					
Higher (at least college)	71 (22.0)	30 (11.8)	2.11	(1.33 to 3.35)	0.001
Family history					
Hypertension	177 (54.8)	114 (44.7)	1.50	(1.08 to 2.09)	0.016
Diabetes mellitus	39 (12.1)	31 (12.2)	0.99	(0.60 to 1.64)	0.98
Stroke	94 (29.1)	52 (20.4)	1.60	(1.09 to 2.36)	0.017
Myocardial infarction	35 (10.8)	22 (8.6)	1.29	(0.74 to 2.24)	0.38
Medical history					
Diabetes	56 (17.3)	54 (21.2)	0.78	(0.52 to 1.18)	0.24
Stroke	13 (4.0)	9 (3.5)	1.15	(0.49 to 2.66)	0.76
Myocardial infarction	13 (4.0)	9 (3.5)	1.15	(0.49 to 2.66)	0.76
Physical findings					
Obesity (BMI >25 kg/m ²)	95 (29.4)	64 (25.1)	1.24	(0.86 to 1.80)	0.25
Concerns about					
Hypertension	289 (89.5)	200 (78.4)	2.34	(1.47 to 3.71)	<0.001
Diabetes	176 (54.5)	121 (47.5)	1.33	(0.95 to 1.84)	0.097
Individual preferences					
Salt preference	206 (63.8)	145 (56.9)	1.34	(0.95 to 1.87)	0.15
Current lifestyle					
Smoking	39 (12.1)	25 (9.8)	1.26	(0.75 to 2.14)	0.39
Drinking	118 (36.5);	91 (35.7)	1.04	(0.74 to 1.46)	0.83
Regular exercise	159 (49.2)	129 (50.6)	0.95	(0.68 to 1.31)	0.75
Reduced salt intake	236 (73.1)	185 (72.5)	1.03	(0.71 to 1.48)	0.89

BMI, body mass index.

Table 4 Multivariate analysis of associations between family history and willingness to undergo genetic testing

	Participants without hypertension			Participants with hypertension		
	Ad-OR	95% CI	p	Ad-OR	95% CI	p
Education						
Higher (at least college)	1.45	(1.13–1.86)	0.003	1.81	(1.12 to 2.93)	0.015
Family history						
Hypertension	1.52	(1.17–1.98)	0.001	1.25	(0.88 to 1.76)	0.21
Stroke				1.55	(1.04 to 2.31)	0.031
Concerns about						
Hypertension	2.03	(1.53–2.68)	<0.001	2.04	(1.27 to 3.28)	0.003
Diabetes	1.10	(0.83–1.44)	0.51			

 Bold font indicates significantly different between groups.
 Ad-OR, adjusted OR.

should be aware of this dependence and should provide care accordingly.

Higher education and anxiety related to hypertension were independently associated with a willingness to undergo genetic testing irrespective of the presence of hypertension. Similarly, a previous study demonstrated that people with college or graduate education had higher awareness of the breast cancer genes BRCA1 and BRCA2 and of tests for these genes.²² Furthermore, higher knowledge level and education showed significant positive correlations with interest in and awareness of breast cancer and ovarian cancer genetic testing.^{23 24} Higher education (postcollege education) is also significantly associated with concerns related with consumer genetic testing.²⁵ Similar to a previous study demonstrating that worry about bowel cancer was a significant factor motivating patients to undergo DNA tests for colorectal cancer,²⁶ our study revealed that concerns related to hypertension were significantly associated with the willingness to undergo genetic testing. These results suggest that higher education and a higher level of related anxiety increase the willingness to undergo genetic testing. Higher education does not always lead to better understanding of the disease²⁷ but may help to more easily understand the limitations of genetic testing. In contrast, those with hypertension seem to have better understanding of the disease because they make efforts to reduce salt intake, stop smoking, refrain from alcohol and engage in regular exercise more than those without hypertension (table 1). Therefore, physicians should consider the extent of a patient's awareness and distress when disclosing the results of genetic tests for salt-sensitive hypertension.

Family history of hypertension was associated with a willingness to undergo genetic testing in patients without hypertension. A previous study reported a similar result; women with a family history of breast cancer had a very high interest in genetic testing for BRCA1 and BRCA2 mutations.⁹ Family history of ovarian cancer also motivated patients to become aware of genetic testing such as that for BRCA.¹⁰ Fortunately, salt restriction reduces blood pressure and prevents cardiovascular events.^{28 29} Therefore, primary care physicians should emphasise the importance of salt restriction when introducing methods for prevention of hypertension to patients.

Family history of stroke was associated with a willingness to undergo genetic testing in patients with hypertension. In previous studies, we did not find evidence supporting an association between genetic predisposition and the onset of the disease for which genetic testing was performed. Hypertension is a well-known risk factor for stroke.¹⁷ Accordingly, such patients worry about the possibility of stroke in the future. In contrast, although hypertension is also a risk factor for myocardial infarction,¹⁸ there was no significant association between family history of myocardial infarction and willingness to undergo genetic testing in this study. In this regard, the incidence of stroke in Japan is four times higher than

that of myocardial infarction.^{30–32} Hence, patients might be more concerned about stroke than about myocardial infarction. Primary care physicians should take into account possible anxiety about the risk of stroke, while counselling patients with hypertension and should not emphasise on only risk of stroke due to the salt-sensitive hypertension. A population-based nationwide campaign might help to successfully reduce dietary sodium intake and prevent cardiovascular events.³³

There are several limitations to this study. First, since all the participants were Japanese, the generalisability of the results may not extend to non-Japanese populations. Mortality from myocardial infarction or stroke differ between populations^{17 34}; the cumulative mortality from heart diseases is lower in Japan than in the USA and other Western countries.³⁰ Family history of myocardial infarction might be associated with a willingness to undergo genetic testing in countries with a high incidence of myocardial infarction. Actually, a population-based survey in the UK showed that respondents with a family history of heart disease were more interested in genetic testing for heart disease than those without.³⁵ Further studies should be conducted to verify this. Second, this study used self-reported data, which might have introduced information bias. For example, it is possible that family history was not correctly reported by less educated patients. Patients are often not well informed about family medical history, and the use of family history in adult primary care has been limited owing to multiple substantive barriers.¹ Third, the patient characteristics used in this study were selected on the basis of previous studies that identified factors associated with a willingness to undergo genetic testing.^{24 36–38} However, unidentified confounding factors may have affected the association between a willingness of undergo genetic testing and family medical history.

CONCLUSIONS

The effect of family history on the willingness to undergo genetic testing for salt-sensitive hypertension depended on whether the individual already had hypertension. Thus, participants without hypertension wished to know the likelihood of developing hypertension in the future, whereas participants with hypertension were interested in knowing their risk of stroke (a complication of hypertension). Family history may be useful when counselling patients about genetic testing on the basis of their medical history.

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Contributors Conceived and designed the experiments: TT, MO, RA and EK. Performed the experiments: TT, MO and MH. Analysed the data: TT and MO. Contributed reagents/materials/analysis tools: TT, MO and RA. Wrote the manuscripts: TT, MO and EK.

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